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Cost-effectiveness of infliximab for the treatment of active and progressive psoriatic arthritis

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A B S T R A C T

Background: Despite its proven efficacy, infliximab is often considered to be an expensive treatment for patients with psoriatic arthritis.
Objectives: To estimate the cost-effectiveness of infliximab among patients with active and progressive psoriatic arthritis.
Methods: A decision analytic model was constructed to simulate disease progression in hypothetical cohorts of patients with psoriatic arthritis receiving infliximab maintenance treatment. The primary response measure was change in Health Assessment Questionnaire score from a baseline estimated from mixed treatment models drawn from published clinical trials. Palliative care, comprising nonbiologic disease-modifying antirheumatic drugs, was used as a comparator. The primary outcome was quality-adjusted life years. The dose of infliximab was estimated for a range of 60 to 80 kg per patient body weight. The costs and outcomes were discounted at 3.5% for a period of 40 years. Uncertainty around the results was explored with probabilistic sensitivity analysis.
Results: The mixed treatment comparison showed a significant reduction in Health Assessment Questionnaire score across all patients. The tumor necrosis factor α inhibitors were significantly superior to palliative care but comparable with one another. The incremental cost-effectiveness ratios for etanercept, adalimumab, and infliximab relative to palliative care were £17,327; £19,246; and £16,942 to £23,022, respectively, across all patients with psoriatic arthritis and £16,613; £18,170; and £15,788 to £21,736, respectively, in the subgroup with significant psoriasis.
Conclusion: Infliximab represents a cost-effective treatment option well within the National Institute for Health and Clinical Excellence threshold relative to palliative care. In light of equivalent outcomes with other tumor necrosis factor α inhibitors, its position in the treatment pathway is likely to be governed by treatment costs.

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Introduction

Psoriatic arthritis is a chronic debilitating spondyloarthropathy characterized by inflammatory arthritis that affects the joints and connective tissue and is associated with psoriasis of the skin or nails. The annual incidence of psoriatic arthritis ranges between 0.1 and 23.1 per 100,000, and the prevalence is estimated to be 1.0 to 420.0 per 100,000 across the globe [1]. The course of psoriatic arthritis can be variable and unpredictable, ranging from a mild and nondestructive disease to an erosive and deforming arthritis (seen in 40% to 60% of patients with psoriatic arthritis) [2]. Patients with untreated psoriatic arthritis may have persistent inflammation, progressive joint damage, severe physical limitations, disability, and increased mortality risk [2]. Psoriatic arthritis carries a significant economic burden, with direct annual medical costs per patient estimated to be €3162 and mean indirect costs per patient estimated to be €11075 in Germany in 2002 [3]. As with most chronic conditions, the major cost drivers of direct costs in psoriatic arthritis are hospitalizations and drug treatments [3,4].

The goals of psoriatic arthritis treatment are to improve disease signs and symptoms; prevent loss of function and disability; prevent or control joint, tendon, and entheses inflammation and damage; and improve quality of life [5,6]. The British Society of Rheumatology guidelines recommend that biologic disease-modifying antirheumatic drug (DMARD) therapy should be used for those patients with active psoriatic arthritis (≥3 tender joints and ≥3 swollen joints) who have no response of their disease to adequate treatment (>6 months) with at least two nonbiologic DMARDs (e.g., methotrexate, sulfasalazine, cyclosporine, or leflunomide) [5].

Tumor necrosis factor α (TNF-α) inhibitors have been shown to be efficacious for patients with psoriatic arthritis who have had treatment failure with at least two DMARDs. Infliximab, a TNF-α inhibitor, has demonstrated significant improvements in the proportion of subjects with achieved and maintained benefits in the rheumatoid and psoriatic components of the disease during a 24-week period in its two randomized, controlled trials, Infliximab Multinational Psoriatic Arthritis Controlled Trial (IMPACT) and IMPACT2 [7,8]. TNF-α inhibitors in general and infliximab in particular are often considered to be costly treatment alternatives, however, and decision makers often challenge their value in treating patients with psoriatic arthritis.

This economic evaluation was performed to assess the cost-effectiveness of infliximab maintenance treatment at the licensed dose of 5 mg/kg in comparison with palliative care without infliximab and other TNF-α inhibitors for the treatment of patients with active and progressive psoriatic arthritis who have had treatment failure with at least two DMARDs. A separate analysis was also performed for the subgroup of patients with psoriatic arthritis who demonstrated a significant psoriatic component at baseline, defined as psoriasis affecting body surface area (BSA) of at least 3%.

Methods

Patients and interventions

The economic analysis focused on patients with active and progressive psoriatic arthritis, among whom two-thirds had significant psoriasis at baseline, with the patient population being based on that studied in infliximab clinical trials (IMPACT and IMPACT2) [7,8]. The effect of a TNF-α inhibitor on the rheumatic component of the disease across all patients was estimated by means of the Health Assessment Questionnaire (HAQ) score. In the subgroup with significant psoriasis at baseline, the effect on the psoriatic component of the disease was also estimated with psoriasis area severity index (PASI). For the a third of the patients with psoriatic arthritis who showed no clinically significant psoriasis (affected BSA <3%), only the impact on the rheumatic component was modeled. For the cohort of patients with psoriatic arthritis, a mean HAQ score of 1.14 (range 0–3) was assumed at baseline. For the two-thirds with significant psoriasis at baseline, a mean PASI score of 11 (range 0–32) was assumed. Patients entered the model at the age of 45 years, and 50% were men.

The analysis compared four treatment alternatives. These included maintenance treatment with a TNF-α inhibitor (infliximab, adalimumab, or etanercept) followed by a sequence of nonbiologic DMARDs or palliative care comprising only nonbiologic DMARDs. The analysis was conducted with a time horizon of 40 years, and half-cycle correction was applied.

Model overview

The model structure in terms of the cohort flow is displayed in Figure 1 and is based on the model previously developed by Bravo Vergel et al. [9]. The main distinction between our model and that used previously is the explicit consideration of the psoriatic component of the condition. The model can be summarized as having a first cycle starting at 0 and running to 12 weeks, a second cycle of 13 to 24 weeks, and annual cycles thereafter. In contrast to the Bravo Vergel et al. model [9], a second cycle of 12 weeks stretching from week 13 to week 24 was included on the basis of trial analysis of infliximab trials suggesting that improvements in the rheumatic and psoriatic components of the disease continue beyond the initial 12 weeks. At the end of the first cycle, all patients were assessed for their Psoriatic Arthritis Response Criteria (PsARC) response. Those who had response to treatment continued with the current treatment, whereas those without response had the treatment withdrawn and moved on to palliative care.

Efficacy estimates and transitions

The efficacy estimates were derived with the incremental treatment effects for the comparative treatments (infliximab, etanercept, and adalimumab). Because no head-to-head trials between TNF-α inhibitors were available, evidence synthesis was undertaken with Bayesian indirect comparison tech-

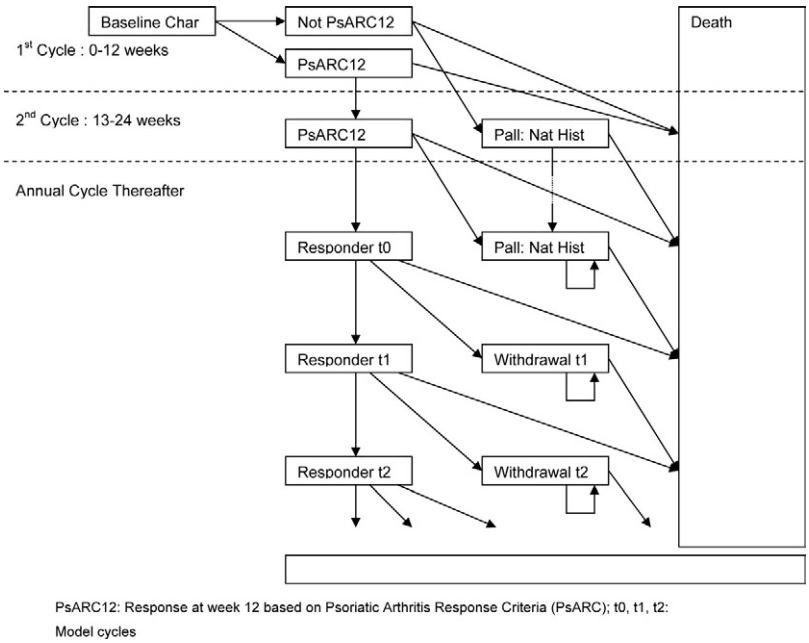

Fig. 1 – Economic model structure. *Char*, characteristics; *PsARC12*, response at week 12 according to PsARC; *Pall*, palliation; *Nat Hist*, natural history; *t0*, *t1*, *t2*, model cycles.

niques. The analysis was conducted with Winbugs/OpenBUGS version 3.0.3, and the code is available in Appendix A found at: 10.1016/j.jval.2010.10.016. Noninformative priors were used for all parameters, and sensitivity to the choice of priors was assessed by rerunning the analysis for different priors. The results did not vary substantially (i.e., the posteriors are dominated by the data and not by the choice of prior). Sampling convergence was verified with the Brooks-Gelman-Rubin diagram. The results were then used in the economic model to estimate the cost-effectiveness of TNF-α inhibitor treatments in patients with psoriatic arthritis.

The network of evidence used is displayed in Figure 2, and the data used in the indirect comparison are displayed in Appendix B found at: 10.1016/j.jval.2010.10.016. The outcomes of interest were PsARC response, the effect on HAQ score and, in the subgroup of patients with BSA at least 3% at baseline, the effect on PASI score. Clinical trial data from the last data points before the early escape were used. The PsARC response was modeled with the probability of a PsARC response with placebo and a treatment-related increment, which was assumed to be on the log-odds scale. Similarly, the change in HAQ score from baseline was modeled conditional on PsARC response with placebo plus a treatment-related increment, separately among those with and without PsARC response. For the subgroup of patients with significant psoriasis, the change in PASI score was also modeled as placebo plus a treatment-related increment but without conditioning on PsARC response. The PASI score change was assumed to be unrelated to PsARC response on the basis of the analysis of patient level data from IMPACT and IMPACT 2.

Beyond the first cycle, the model assumed continued HAQ score reduction for patients responding to treatment for the first three cycles (12, 12, and 52 weeks). The assumption was based on the analysis of IMPACT and IMPACT 2, which estimated the incremental HAQ score reductions among those with treatment responses to be -0.0628 and -0.0313 relative to those with placebo responses in the second and third cycles, respectively. This HAQ score reduction was estimated for infliximab. In the absence of any data on differential HAQ score reduction among TNF-α inhibitors, identical estimates were used for all treatments. For patients withdrawing from treatment, rebound was assumed to occur within one cycle and estimated to be equal to gain, with natural history disease progression thereafter (Curve A-C-D-E-F). This assumption was further explored in one-way sensitivity analysis, wherein the rebound was assumed to be equal to the natural history

Study	Placebo	Infliximab	Etanercept	Adalimumab
Antoni 2005a[7]	PsARC/PASI	PsARC/PASI		
Antoni 2005b[8]	PsARC/HAQ/PASI	PsARC/HAQ/PASI		
Mease 2000[20]	PsARC/PASI		PsARC/PASI	
Mease 2004[21]	PsARC/PASI		PsARC/PASI	
Mease 2005[20]	PsARC/HAQ/PASI			PsARC/HAQ/PASI
Genovese 2007[23]	PsARC/HAQ			PsARC/HAQ
Bravo Vergel 2006[9]	HAQ	HAQ	HAQ	

Fig. 2 – Network of evidence used for PsARC, HAQ, and PASI responses.

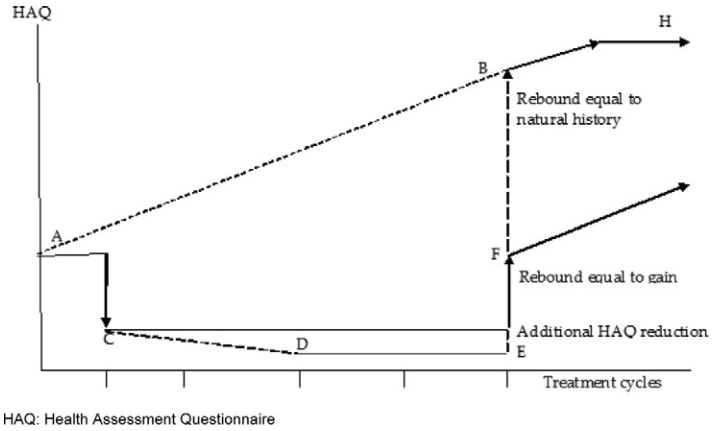

Fig. 3 – HAQ score reduction and rebound effect.

disease progression with only palliative care (Curve A-B). These scenarios are depicted in Figure 3. The natural history disease progression for HAQ score was derived from the Leeds NESPAR study and was estimated to be 0.0719 per year [9]. In the case of PASI score, the model assumed a flat PASI score benefit beyond the initial decrement in the first cycle. This assumption was based on expert opinion, which also suggested no natural history PASI score progression for patients not treated with TNF-α inhibitor therapy. For patients with lost response, the PASI score was assumed to rebound back to baseline within a cycle of withdrawal and remain at that value.

Beyond the first cycle, all patients had an annual probability of 11.14%, identical for all treatment alternatives, of withdrawal from treatment and moving onto palliative care [10]. The Geborek et al. study [11] estimated the withdrawal rates for etanercept and infliximab for a 17-month period in which 43 patients out of 279 withdrew from TNF-α inhibitor treatment. The probability of death was estimated for the general population and adjusted with psoriatic arthritis mortality multipliers of 1.60 for female patients and 1.66 for male patients [11].

Costs

Perspective

The perspective adopted for costs was that of the National Health Service in England and Wales. The reference year used for costs was 2008, with all costs except the drug costs being inflated according to Personal Social Services Research Unit inflation indices. Productivity losses, although significant, were omitted because of this choice of perspective.

Drug administration and monitoring costs

The total cost of infliximab treatment was broken down into its acquisition cost (£419.62 per 100-mg vial) taken from the British National Formulary and administration cost. Because dosing for infliximab is weight dependent, the base case was presented for a range of 60 to 80 kg per patient weight. Patients with body weights within this range were assumed to vial optimize, thus saving significant drug costs. This assumption was based on a survey of rheumatology centers in the United Kingdom suggesting that a majority of all rheumatology patients receive vial optimized infliximab. Treatment costs for other TNF-α inhibitors were also taken from the British National Formulary. The resultant drug costs for the first and subsequent cycles are displayed in Table 1.

For the administration costs, it was assumed that during the first cycle the subcutaneous formulations would require an initial consultant outpatient visit followed by two separate 4-hour nursing staff visits to educate the patient in self-administered injections, together costing £394.09 per patient. The infusion cost used for infliximab was £124 per infusion according to a previous appraisal [12]. On an ongoing basis, the subcutaneous TNF-α inhibitors were assumed to require two outpatient visits coupled with 1 hour of staff nurse time for monitoring in each subsequent year, together costing £309.06 per patient. The corresponding resource use for infliximab was a single outpatient visit costing £135.71 per patient per year. Because of the hospital-based dosing, it was assumed that infliximab monitoring costs would be incurred during infusion administration, and thus no additional costs were applied. All TNF-α inhibitors were assumed to be accompanied by annual laboratory tests costing £82.65 per patient.

Ongoing costs

The ongoing costs were estimated as a function of HAQ score for the third of patients with no psoriatic component and as a

Table 1 – Drug costs.

	1st cycle	2nd cycle	Annual thereafter
Infliximab (60–80 kg)	£3776.58 to £5035.44	£2517.72 to £3356.96	£8182.59 to £10910.12
Etanercept	£2145.12	£2145.12	£9295.52
Adalimumab	£2145.00	£2145.00	£9295.00

function of HAQ and PASI scores for the remaining two-thirds of patients. The cost per HAQ score change regression derived from a study by Kobelt et al. [13] estimated a resource use cost of £401 (SE £259) per point increase in HAQ score per year with a constant of £1325 (SE £466). In line with the Bravo Vergel et al. model [9], patients continuing treatment were assumed to incur 85% of these costs, whereas those withdrawing from treatment and moving on to palliative care were assumed to incur 100% of these costs [9]. The cost as a function of PASI score was derived from a survey of 20 dermatologists. The respondents were selected by stratified sampling according to geography, size of the practice, clinic setup (coclinic with rheumatology vs. separate), and previous experience with TNF-α inhibitors. A majority of the questions in the survey were closed ended and asked the respondents to estimate the resource use for a range of PASI scores (<5, 5–9, 10–19, 20–29, >29). The responses were then used to estimate the resource use costs, including the dermatology inpatient, consultant-led outpatient, nurse-led outpatient, and phototherapy costs according to PASI scores. On the basis of the results, an additional cost of £167 per PASI score point increase was applied for the subgroup of patients with significant psoriasis at baseline.

Outcomes

The primary outcome was quality-adjusted life years (QALYs), estimated as a function of both the HAQ and the PASI scores. The literature search did not identify any utilities for patients with psoriatic arthritis estimated directly with EQ-5D or SF-6D. Therefore two indirect methods published in the literature with SF-36 (SF-12) mapping to EQ-5D and then on to utilities [14] and SF-36 (SF-6D) mapping directly to utilities [15] were used. The current National Institute for Health and Clinical Excellence (NICE) Methods Guide explicitly prefers EQ-5D, and we therefore selected the Gray algorithm in the base case, with the Brazier algorithm being explored in the sensitivity analysis [16]. The regression models based on these algorithms are displayed in Table 2.

Cost-effectiveness analyses

The results of the cost-effectiveness analysis are reported here in the form of incremental cost per QALY gained. Costs and outcomes were calculated separately for each treatment alternative and were discounted at 3.5% per annum, in accordance with the NICE guidelines [16]. In the base case, the cost-effectiveness was estimated for all patients with psoriatic arthritis. A separate subgroup analysis was conducted for patients with significant psoriasis at baseline (BSA >3%). Multiple one-way sensitivity analyses were conducted, varying the parameters such as baseline HAQ and PASI scores, time horizon, HAQ score reduction beyond first cycle, withdrawal rates, natural history HAQ score progression, and utility estimates to assess the structural and parametric uncertainty around the model results. The uncertainty surrounding important variables was further explored with probabilistic sensitivity analyses with 5000 simulations. In the probabilistic sensitivity analyses, the PsARC response, the HAQ and PASI score changes conditional on PsARC response, the withdrawal rates, the psoriatic arthritis mortality multipliers, and the utilities were modeled with β distributions. The natural history disease progression and cost as a function of HAQ or PASI score were implemented with a normal distribution subject to a non-negative value.

Results

Cost-effectiveness analyses

The results of the network meta-analysis used in the model are displayed in Table 3. The results showed that all TNF-α inhibitors were significantly superior to palliative care for PsARC response in all patients and PASI score improvement among patients with significant psoriasis. In addition, infliximab and etanercept were superior to palliative care for HAQ score improvement. Among the TNF-α inhibitors, infliximab and etanercept were broadly similar, with infliximab being numerically superior with regard to PsARC response and PASI score improvement and etanercept being numerically better with regard to HAQ score improvement. Both infliximab and etanercept were superior to adalimumab with regard to PsARC response but comparable with regard to other outcomes.

The analysis estimated that less than 50% of patients were receiving TNF-α inhibitor treatment by the end of the fourth year, and less than 1% were receiving treatment by the end of model time horizon. The costs and benefits associated with each treatment and the resulting incremental analyses for all patients with psoriatic arthritis and those with significant

Table 2 – Utility estimation algorithms.

	Brazier algorithm		Gray algorithm	
Covariate	Mean	SE	Mean	SE
Intercept	0.6373442	0.0044571	0.6442260	0.0115177
sHAQ	−0.0976821	0.0034040	−0.1610008	0.0087963
sPASI	−0.0253398	0.0051215	−0.0375632	0.0132345
$sHAQ^2$	0.0111282	0.0025956	−0.0050072	0.0067073
$sPASI^2$	0.0040523	0.0011751	0.0051515	0.0030365

sHAQ = (HAQ − 0.85730)/0.66497. sPASI = (PASI − 5.13489)/7.30676. SE, standard error of the mean.

Table 3 – Results of the network meta-analysis.

Outcome	Placebo (mean ± SE, 95% CI)	Infliximab (mean ± SE, 95% CI)	Etanercept (mean ± SE, 95% CI)	Adalimumab (mean ± SE, 95% CI)
PsARC response	0.261 ± 0.021 (0.220, 0.304)	0.769 ± 0.036 (0.695, 0.835)	0.748 ± 0.041 (0.663, 0.823)	0.586 ± 0.038 (0.509, 0.658)
HAQ score change from baseline, PsARC responders	−0.268 ± 0.061 (−0.383, −0.146)	−0.636 ± 0.073 (−0.790, −0.502)	−0.705 ± 0.077 (−0.853, −0,552)	−0.458 ± 0.128 (−0.705, −0.203)
HAQ score change from baseline, PsARC nonresponse	0.016 ± 0.031 (−0.048, 0.075)	−0.167 ± 0.059 (−0.285, −0.056)	−0.212 ± 0.071 (−0.351, −0.073)	−0.184 ± 0.133 (−0.446, 0.078)
PASI score change from baseline, BSA ≥3% subgroup	0.752 ± 0.515 (−0.196, 1.734)	−6.585 ± 0.924 (−8.345, −4.839)	−4.070 ± 0.826 (−5.692, −2.551)	−5.358 ± 3.924 (−14.09, 2.541)

SE, standard error of the mean; CI, confidence interval.

psoriasis are displayed in Table 4. The results demonstrated that for a typical patient with psoriatic arthritis weighing as much as 100 kg, all three TNF-α inhibitors were cost-effective relative to palliative care. The incremental cost-effectiveness ratios (ICERs) for etanercept, adalimumab, and infliximab relative to palliative care were £17,327; £19,246; and £16,942 to £23,022, respectively, across all patients with psoriatic arthritis and £16,613; £18,170; and £15,788 to £21,736, respectively, in the subgroup of patients with significant psoriasis at baseline.

Sensitivity analyses

The results of one-way sensitivity analysis are displayed in Table 5. Results were sensitive to change in structural assumptions such as utility estimates and HAQ score rebound after TNF-α inhibitor withdrawal, as well as parametric modifications such as halving the rate of natural HAQ score progression, resulting in ICERs greater than £30,000/QALY. The effects of changes in other parameters, such as discount rate (0–6%), sex, and model time horizon, were less significant. The results of the probabilistic sensitivity analyses suggest infliximab to be cost-effective with a willingness to pay that could be as low as £12,000 for typical patients with psoriatic arthritis, as displayed in Figures 4A and 4B.

Table 4 – Base case results for patient weight of 60 to 80 kg.

	Total QALYs	Total costs	ICER vs. palliative care
All patients			
Palliative care	6.10	£64,704	—
Adalimumab	7.89	£99,278	£19,246
Etanercept	8.62	£108,481	£17,327
Infliximab	8.65	£107,954–£123,475	£16,942–£23,022
Psoriasis patients			
Palliative care	5.79	£76,402	—
Adalimumab	7.63	£109,682	£18,170
Etanercept	8.35	£118,925	£16,613
Infliximab	8.40	£117,606–£133,128	£15,788–£21,736

Discussion

Infliximab is an efficacious treatment alternative for patients with active and progressive psoriatic arthritis [7,8]. The objective of this analysis was to assess the cost-effectiveness of infliximab treatment at the licensed dose of 5 mg/kg in patients with psoriatic arthritis. Three studies in the literature have estimated the cost-effectiveness of TNF-α inhibitors in psoriatic arthritis [9,17,18]. All three studies adopted models reported in the literature for rheumatoid arthritis and used rheumatoid arthritis data for key parameters, such as the relationship between HAQ score and costs. None of the studies, however, captured the impact of TNF-α inhibitors in improving the symptoms of psoriasis, thus excluding the benefit arising from treating psoriasis. The study by Olivieri et al. [18] captured the benefit of TNF-α inhibitors for a period of 6 months after treatment initiation, whereas the other two studies used models that extended beyond the trial period and out to 10 years. For a chronic condition such as psoriatic arthritis, capturing the benefits over the lifetime of the patient may be more appropriate. The study by Bravo Vergel et al. [9] compared infliximab and etanercept with each other and with standard care, whereas the other two studies only compared the TNF-α inhibitor with standard care. Also, none of the studies included adalimumab as a treatment alternative. We attempted to address these limitations of the previous works in our analyses. We selected the model structure developed by Bravo Vergel et al. [9] because it was deemed to be the most appropriate and robust analysis in a previous NICE appraisal [19]. Our results indicated the cost-effectiveness of TNF-α inhibitors to be in the range of £17,327 to £23,022 per QALY, which is lower than values reported in the literature [9,17,18]. This may be attributable to a variety of factors, including accounting for the TNF-α inhibitor benefit in psoriasis and lifetime estimates of costs and benefits.

TNF-α inhibitors when compared with each other showed little difference in effectiveness. Adalimumab was significantly worse with regard to the PsARC response but only numerically inferior with respect to HAQ and PASI score changes relative to the other two TNF-α inhibitors. Our network meta-analysis used patient-level data from in-

Table 5 – Results of one-way sensitivity analyses (patients with psoriasis).

Parameter change	ICERs vs. palliative care		
	Etanercept	Adalimumab	Infliximab 60–80 kg
Reducing baseline HAQ score from 1.14 to 0.90	£17,170 (£16,464)	£18,984 (£17,927)	£16,774–£22,797 (£15,634–£21,527)
No HAQ score change beyond first cycle	£18,686 (£17,903)	£20,932 (£19,736)	£18,304–£24,832 (£17,035–£23,410)
Reducing baseline PASI score from 11.0 to 9.0	£17,289 (£16,558)	£19,184 (£18,083)	£16,882–£22,940 (£15,705–£21,621)
Applying 20-year time horizon	£21,229 (£20,309)	£24,148 (£22,710)	£20,874–£28,247 (£19,381–£26,560)
Rebound equal to natural history	£29,356 (£27,944)	£35,968 (£33,487)	£28,989–£39,029 (£26,682–£36,365)
Halving annual withdrawal from TNF-α inhibitor treatment from 11.14% to 5.6%	£18,101 (£17,340)	£20,254 (£19,095)	£17,406–£23,658 (£16,183–£22,292)
Halving rate of HAQ score progression under natural history from 0.072 to 0.036	£24,497 (£23,399)	£28,619 (£26,827)	£24,112–£32,552 (£22,318–£30,508)
Applying Brazier algorithm for quality of life	£37,337 (£35,603)	£44,262 (£41,372)	£36,870–£50,095 (£34,026–£46,843)

fliximab clinical trials and used published meta-analysis results for etanercept drawn from patient-level information [10,20,21]. Such information was not available for adalimumab, however, and we used published trial results [22,23]. These results may have contributed to adalimumab being significantly worse with regard to PsARC response. Because the TNF-α inhibitors were similar with regard to the efficacy results, we treated them as a class and did not

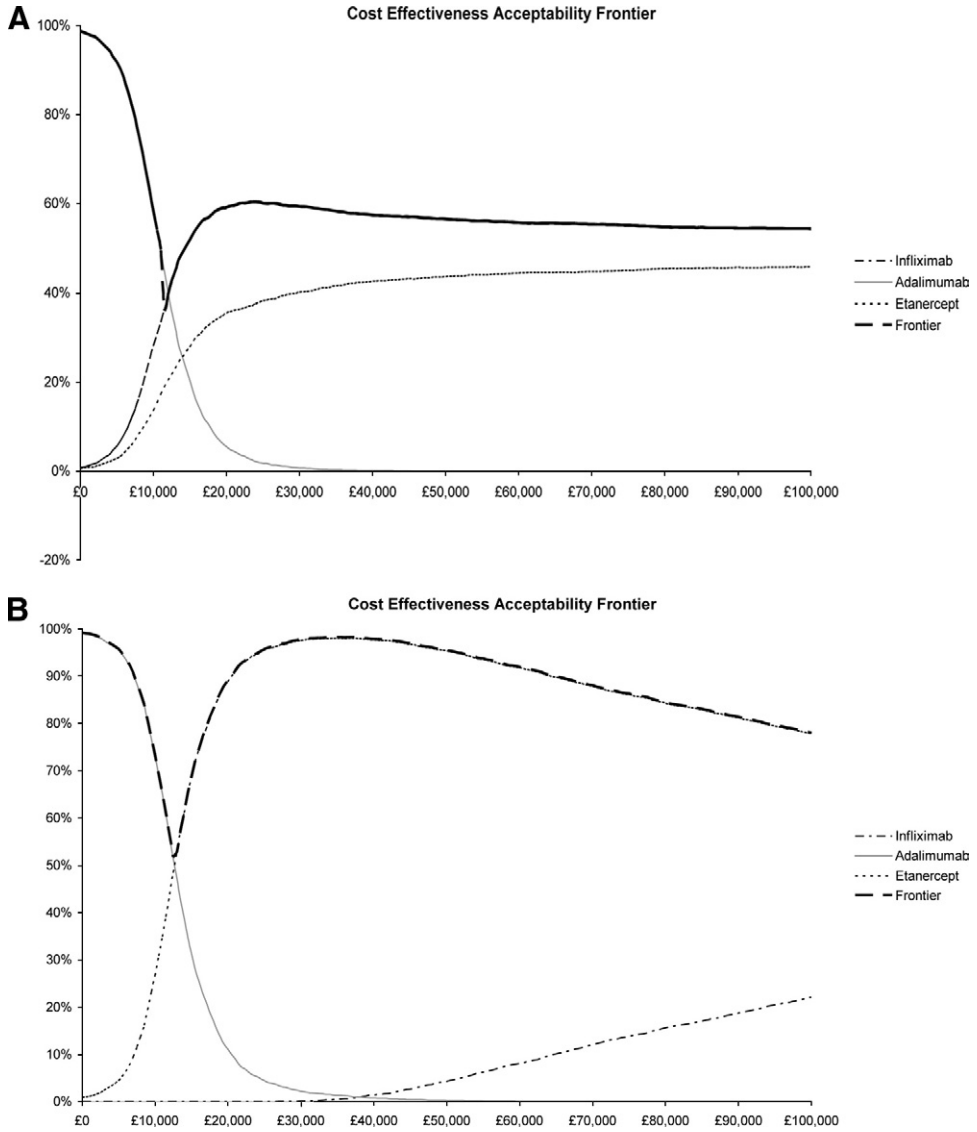

Fig. 4 – (A) Cost-effectiveness acceptability curves and frontier for 60-kg patient. (B) Cost-effectiveness acceptability curves and frontier for 80-kg patient.

present ICERs comparing them. Similar efficacy resulting in small incremental benefit may produce a wide range of ICERs, from being dominant to very high, especially when comparing infliximab and etanercept. The uncertainty increases further particularly depending on the assumptions around rebound effect and the quality of life algorithm. This lack of consensus regarding methods and assumptions translates into considerable uncertainty around cost-effectiveness results. Further research is needed to address some of these uncertainties. In light of this, the treatment costs, including the cost of drug acquisition, are likely to play a significant role in the choice of TNF-α inhibitor. It is important to note that our interpretation of results is in direct contradiction to the current NICE guidance, which recommends adalimumab and etanercept ahead of infliximab for treatment of psoriatic arthritis [19,24]. It is also important, however, to consider the context in which NICE made that decision. The Bravo Vergel et al. [9] analysis that informed the NICE appraisal committee did not incorporate the psoriatic benefit of TNF-α inhibitors. As a result, the ICERs for etanercept and adalimumab were below the acceptability threshold of £30,000/QALY, whereas the ICER for infliximab was above the threshold. This may have influenced NICE to recommend etanercept and adalimumab ahead of infliximab. Our analysis suggests that all the TNF-α inhibitors have ICERs well below the acceptability threshold and therefore should be considered as appropriate treatment alternatives, even within the NICE constraints. This is likely to be reflected in the NICE's decision on an ongoing appraisal of TNF-α inhibitors in psoriatic arthritis [25,26].

The sequence of treatments modeled is an important consideration in psoriatic arthritis. We did not include sequential treatment with a second TNF-α inhibitor for patients with primary nonresponse or those withdrawing from treatment. This was primarily because of unavailability of psoriatic arthritis–specific data on sequential use. Our model was based on that used by Bravo Vergel et al. [9], and we made the necessary structural and parametric changes to incorporate new evidence. The important modifications included adding in a second cycle of 12 weeks stretching from week 13 to week 24 and the additional assumptions regarding continued HAQ score reduction up to the third cycle. These modifications were based on the clinical trial analysis of infliximab, which suggested continued improvements in rheumatoid and psoriatic components among those with treatment response. In the absence of any similar evidence regarding other TNF-α inhibitors, however, the comparative ICERs should be interpreted with caution. We also excluded the adverse events from our analysis. The clinical trials have demonstrated that the adverse events associated with TNF-α inhibitors are infrequent, minor, and not significantly different from those associated with palliative care. We therefore would not anticipate adverse events to have a significant impact on the costs or QALYs and thus on the final results. On the contrary, the utility estimation method significantly affects the ICERs. We selected EQ-5D in the base case because it is recommended by NICE and has been used in previous analyses. We believe that EQ-5D is a more appropriate scale in psoriatic arthritis because of its domains (mobility, self-care, usual activities, and pain), which capture highly relevant information on parameters affecting a patient with psoriatic arthritis. The use of utilities derived from SF-36, however, significantly increases the ICERs.

The rebound assumption after treatment withdrawal is also an important one. We assumed rebound equal to gain in our base case analysis and explored the surrounding uncertainty in sensitivity analysis. The ICERs increased but were still within the acceptable range for patients receiving etanercept and a proportion of those receiving infliximab. With no conclusive evidence of rebound effect in the literature, however, it is difficult to ascertain the true impact of this assumption on the resultant ICERs. Similarly, in absence of any data in literature regarding PASI score natural progression and PASI score rebound after loss of response, we assumed PASI score would remain constant as long as the patient had a response and would revert back to baseline after loss of response. This is in accordance with a recent NICE appraisal [25]. Because of the lack of any available data, it is impossible to determine whether this assumption is optimistic or conservative and how much the PASI score should be varied with time to estimate the underlying uncertainty. Any such sensitivity would have contributed equally to all TNF-α inhibitors, however, and would have minimal impact on their positioning relative to palliative care. We therefore did not explore the uncertainty around this assumption in our sensitivity analysis. Our results are also sensitive to the number of infliximab vials used per infusion and the assumption of vial optimization. We provided a range of results derived for a mean patient weight in the range of 60 to 80 kg. Despite the uncertainty outlined here, infliximab moves further away from subcutaneous TNF-α inhibitors for patients with psoriatic arthritis weighing less than 60 kg or more than 80 kg. These are important parameters that may influence the treatment choice among TNF-α inhibitors.

Conclusion

Infliximab is an effective and well-tolerated therapy for the management of patients with active and progressive psoriatic arthritis and provides significant clinical benefit with respect to palliative care. Economic analyses demonstrate that the incremental costs associated with achieving these benefits are reasonable and that infliximab may represent a cost-effective treatment option well within the NICE threshold relative to palliative care without biologic DMARDs. Because of equivalent outcomes with other TNF-α inhibitors, the position of infliximab in the treatment pathway within a resource-constrained health system is likely to be governed by treatment costs.

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at 10.1016/j.jval.2010.10.016.

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